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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,146	04/27/2005	Joseph K Belanoff	019904-003210US	5372

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EXAMINER	
ROGERS, JUNE MARIE	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,146	BELANOFF, JOSEPH K	
	Examiner	Art Unit	
	JUNE ROGERS	4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 12-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/15/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-5 and 12-16, in the reply filed on 11/07/2007 is acknowledged. Applicant's specie election of 17-beta-hydrox- 17-alpha- 19-(4-methyl-phenyl)-androsta-4,9 (11)-dien-3-one) filed on December 13, 2007 is acknowledged. The traversal is on the ground(s) that all glucocorticoid receptor antagonists are all effective for treating migraines because they prevent agonist binding to the glucocorticoid receptor. This is not found persuasive because the structure of a particular glucocorticoid receptor antagonist affects the affinity of the antagonist for the receptor; therefore the efficacy of binding will be different from one glucocorticoid compound to the next, i.e. a partial antagonist verses a full antagonist. This difference in binding is often enough to make one compound more effective than another when treating receptor mediated conditions and diseases.

The requirement is still deemed proper and is therefore made ***FINAL.***

Priority

This application claims priority to US Provisional Application No. 60/424/199, filed on November 5, 2002. Applicant's priority is acknowledged.

Status of Claims

Claims 6-11 and 17-21 have been cancelled. Claims 1-5 and 12 are under examination in this application.

Claim Rejections - 35 USC § 112 (Scope of Enablement)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 and 12-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of migraine with a glucocorticoid receptor antagonist ***with*** progesterone receptor binding activity (RU-486/mifepristone), does not reasonably provide enablement for treatment of migraine with a glucocorticoid receptor antagonist ***devoid*** of progesterone receptor binding activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (Bd Apls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6)

the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention:

The instant invention relates the use of steroidal glucocorticoid receptor antagonists devoid of progesterone receptor binding activity in the treatment of migraines.

The relative skill of those in the art:

The relative skill of those in the art is high, with a typical practitioner having obtained a PhD, M.S., MD or equivalent advanced degree.

The breadth of the claims

The instant claims are deemed very broad since the generic description of the compounds encompasses numerous compounds with divergent structures, properties and functionality.

The predictability or lack thereof in the art and the amount of direction or guidance presented:

It is noted that the pharmaceutical art/treatment is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses h compositions with varying effects

and unknown side effects. As such, each composition will need to be individually evaluated for activity.

The description of a steroidal glucocorticoid receptor antagonist devoid of progesterone receptor binding activity includes the possibility of hundreds of compounds with divergent chemical properties. Even the substitution of one atom by another often results in divergent chemical properties and unpredictable treatment efficacy.

The presence or absence of working examples the quantity of experimentation necessary:

Applicant provides several examples for the treatment of migraines with a steroidal glucocorticoid receptor antagonist ***with*** progesterone receptor binding activity (mifepristone, i.e. RU-486). However, this description does not enable one of skill in the art to use a steroidal glucocorticoid receptor antagonist devoid of progesterone receptor binding activity in the treatment of migraines. There are no other compounds shown to have the ability to treat migraines. Note that the court of In re Curtis held that "a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when, the evidence indicates ordinary artisans could not predict the operability.....of any other species." (emphasis added, see In re Curtis 354 F.3d 1347, 69 USPQ2d 1274, Fed. Cir. 2004).

The lack of working examples is a critical and crucial factor to be considered, especially in cases involving an unpredictable and undeveloped art. See MPEP § 2164. Thus, the specification fails to provide clear and convincing evidence in sufficient

support of the use of steroidal glucocorticoid receptor antagonists devoid of progesterone receptor binding activity in the treatment of migraines Genentech, 108 F.3d at 1366, states that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors as discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamanaka et al. (US 6,589,974), Morris et al. (US 2003/0148987) and the Merck Manual.

Hamanaka et al. discloses a method of treating glucocorticoid mediated diseases comprising the administration, to a human a composition comprising a glucocorticoid receptor antagonist, wherein the diseases include pain such as headache (abstract, col.

1, line 62 to col. 2, line 54). Hamanaka et al. teaches the composition can be administered in a variety of dosage forms such as tablets, powers, lozenges, syrups (col. 45, lines27-30) and transdermal (col. 45, line 61). Hamanaka et al teaches the glucocorticord receptor antagonist is employed in the composition from about 0.1ug/kg to about 500mg/kg of body weight (col. 46).

Morris et al. teach that migraine is associated with glucocorticoid and may be treatable by a glucocorticoid receptor antagonist (paragraphs 0028-0031, 0038). Morris et al. further teaches that glucocorticoid amplify the vasoconstrictive actions (paragraph 0023). Merck Manual reveals that migraine is characterized by headache and may be due to intracerebral vasoconstriction (1355-1356).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to use a glucocorticoid receptor antagonist for the treatment of migraine. A person of ordinary skill in the art would have been motivated to a glucocorticoid receptor antagonist for treatment of migraine because migraine is known to be associated to glucocorticoid, particularly, glucocorticoid amplify vasoconstrictions which may cause migraine, and glucocorticoid receptor antagonists is known to be useful for treating pain particularly, headache, which is the symptoms of migraine.

As to Applicant's claims 3-5 and 14, optimization of a result effective parameter, e.g., the timing for the administration of a therapeutic agent, is considered within the skill of the artisan. See, In re Boesch and Slanev (CCPA) 204 USPQ 215.

It is noted that the prior art is silent as to whether or not the glucocorticoid

receptors are devoid of progesterone activity; however, the limitation of being devoid of progesterone activity is not given patentable weight in the absence of a showing by Applicant that glucocorticoid receptor antagonists devoid of progesterone activity provide unexpected results in the treatment of migraines verses a glucocorticoid receptor antagonist with progesterone binding activity. Until such a showing, it is the position of the Examiner that all glucocorticoid receptors, regardless of progesterone binding activity, can be used to treat migraines, as disclosed in the prior art.

Conclusion

No claims allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JUNE ROGERS whose telephone number is (571)270-3497. The examiner can normally be reached on M-F 9-6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Juné M. Rogers

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614